PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

SCHAEFER, Konrad
Schaefer & Emmel
Gehölzweg 20
D-22043 Hamburg
ALLEMAGNE

PATENTANWÄLTE SCHAEFER & EMMEL
EING. 10. Juni 1999
REG.
FRIST 11.6.F.

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	08.06.99
Applicant's or agent's file reference 01110eppc	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP98/00917	18/02/1998	21/02/1997

Applicant
KANTON ZURICH et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Hingel, W Tel.(+49-89) 2399-8717

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
01110eppc		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP98/00917	18/02/1998	21/02/1997
International Patent Classification (IPC) or national classification and IPC C12N15/70		
Applicant KANTON ZURICH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17/08/1998	08.06.99
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Ury, A Telephone No. (+49-89) 2399 8411

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP98/00917

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-43 as originally filed

Claims, No.:

1-39 as originally filed

Drawings, sheets:

1/9-9/9 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 18, 19, 34.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 18, 19, 34 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2, 8-13, 15-17, 21, 24-27, 29-33, 35-39
	No:	Claims	1, 3-7, 14, 20, 22-23, 28
Inventive step (IS)	Yes:	Claims	2, 8-11, 15-17
	No:	Claims	1, 3-7, 12-14, 20-33, 35-39
Industrial applicability (IA)	Yes:	Claims	1-35, 37, 39
	No:	Claims	

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Item III.

Claims 18, 19 and 34 are of such unclear nature that their examination for novelty, inventive step and industrial applicability is virtually impossible.

N.B.: Even if claim 34 was to read "A method...22 and 23 ***is used***" the claim would still not be clear since no immunological detection of a disease-specific PrP (i.e. a protein) can be obtained when said protein is treated with a recombinant prion protein (i.e. another protein).

Item IV.

The application lacks unity within the meaning of Rule 13 PCT for the following reasons.
The separate inventions/groups of inventions are based on the subject-matter of:
- claims 8 and 15,
- claims 9 and 16,
- claims 10 and 17.

The common concept linking together independent claims 8-10 and 15-17 is the following:
Monoclonal antibodies (and the corresponding hybridoma cell lines) reacting with certain epitopes of PrP. This common concept is not novel, see e.g. document D1 which discloses such mABs.
Thus, said groups of inventions are not so linked as to form a single general inventive concept. No technical relationship which finds expression in the claims in terms of the same or corresponding special technical features (i.e. the particular technical feature(s) that define a contribution over the prior art) exists between these three groups of inventions.

Even if the method of preparing the hybridoma cell lines (e.g. a method according to claim 25) was inventive, the lack of unity objection would be maintained since the hybridoma cell lines *per se* would still not be linked so as to form a single general inventive concept.

Item V.

Reference is made to the following documents:

D1: KASCSAK et al., Dev. Biol. Stand., 80, 1993, pp.141-151.
D2: KRASEMANN et al., J. Immunological Methods, 199(2), 1996, pp.109-118.

I) Document D1 discloses (see in particular pages 142 and 143) monoclonal antibodies (3F4, 4B4 and 7G5) having the same features as those mentioned for the monoclonal antibodies according to claims 1 and 3-7.
Thus, D1 destroys the novelty (Article 33.2 PCT) of claims 1 and 3-7.
Said monoclonal antibodies are produced by hybridoma cell lines (see D1, page 142, "Antisera"). This destroys the novelty of claim 14 when it refers to claims 1 and 3-7.
The methods for production of said antibodies and hybridoma cell lines as disclosed in claims 24-27 merely involve classical technics which are obvious for the skilled person. Claims 24-27 lack an inventive step under Article 33.3 PCT.

The attention of the Applicant is drawn to the following point. The method of claim 25 involves the use of a recombinant PrP according to claim 22 or 23. The fact that the PrP is defined as being "recombinant" does not *per se* confer to said PrP any distinguishing technical features over the naturally occurring (native) protein. If inventive step of the method of claim 25 should be based on the use of a recombinant protein, the technical features (if any) which characterise such a recombinant PrP should be introduced in the claim.

Dependent claim 12 does not contain any features which, in combination with the features of claim 1 to which it refers, meet the requirements of the PCT in respect inventive step (Article 33.3 PCT).

An antibody raised against the binding region (idiotype) of a known antibody (according to claim 1) is routinely obtained and does not involve an inventive step. Thus, claim 13 does not fulfil the requirements of Article 33.3 PCT when it refers to claim 1.

II) The recombinant expression vectors disclosed in Fig.3 of D2 destroy the novelty of claims 20 and 28.
The PrP ORF was known in the art at the priority date of the present application. Its insertion in the known pET11a vector to obtain pbPrP3 (see the description page 28) does not involve an inventive step. Thus, claim 21 does not fulfil the requirements of Article 33.3 PCT.

Fig. 1 of D2 destroys the novelty (Article 33.2 PCT) of claims 22 and 23.

Claim 29 is not inventive since it merely claims the use of a known expression vector for the production of a known protein encoded by said vector.

III) It would seem that the present application is based on a monoclonal antibody, named 15B3, that can discriminate between the normal (PrP^{C}) and disease-specific (PrP^{Sc}) forms of PrP. In the native state, mAB 15B3 stains only bovine PrP^{Sc} and not PrP^{C} (page 11 and Fig.6b of the application). mAB 15B3 precipitates only PrP^{Sc} from infected cattle, mice or humans, but not PrP^{C} (page 33). mAB 15B3 involves an inventive step (Article 33.3 PCT).
Although mABs 6H4 and 34C9 do not exhibit this conformational epitope specificity for PrP^{Sc}, they were also not derivable in an obvious manner from the cited prior art. However, they do not show a common inventive concept with the mAB 15B3 (see item IV).

In consequence, the subject-matter of claims 2, 8-11, 15-17 fulfil the requirements of Article 33.2 and 3 PCT.

IV) Claim 30-33 and 35-39 relate to classical test kit, immunological detection procedure, pharmaceutical preparation, method for therapy and use of mAB. Said claims are objected to for lack of novelty and/or lack of inventive step when they do not refer to novel and inventive matter (i.e. the specific mABs according to the present application).

V) For the assessment of the present claims 36 and 38 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example,

does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Item VI.

Certain published documents (Rule 70.10)

Application No.	Publication	Filing	Priority
WO 97/10505	20.03.97	13.09.96	14.09.95

Item VIII.

1) The subject-matter of a great many claims do not fulfil the requirements of Article 6 PCT taken in conjunction with Rule 6.3a PCT which states that the subject-matter for which protection is sought must be defined in terms of the **technical features** of the invention.
The claims objected to are inter alia claims 1-7, 12-14.
Note that these claims (in particular claim 2 which is considered novel and inventive) do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is defined in terms of the result to be achieved which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added.

2) Article 6 PCT requires that the claims shall be clear.
The mAB designations 6H4, 34C9 and 15B3 (claims 8-11) and the plasmid designation pbPrP3 used in claim 7 are arbitrary denominations which are meaningless for third parties since they convey no technical information to the reader of the claims.

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* 01110eppc

Box No. I TITLE OF INVENTION

Immunological Detection of Prions.

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

Kanton Zürich
vertreten durch die Erziehungsdirektion
Walchetor
CH-8090 Zürich

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(i.e. country)* of nationality:

State *(i.e. country)* of residence: CH

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

Korth, Carsten
Lengstraße 70
CH-8008 Zürich

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: DE

State *(i.e. country)* of residence: CH

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation The address must include postal code and name of country.)*

Schaefer, Konrad
Schaefer & Emmel
Gehölzweg 20
D-22043 Hamburg

Telephone No. 040 6562051

Facsimile No 040 6567919

Teleprinter No

☐ Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

Stierli, Beat
Alte Landstraße 38
CH-8114 Dänikon

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: CH

State *(i.e. country)* of residence: CH

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

Streit, Peter
Scheuchzerstraße 9
CH-8006 Zürich

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: CH

State *(i.e. country)* of residence: CH

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

Oesch, Bruno
Haldenstraße 13
CH-5233 Stilli

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: CH

State *(i.e. country)* of residence: CH

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)*

Moser, Markus
Waidfussstraße 25
CH-8037 Zürich

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(i.e. country)* of nationality: CH

State *(i.e. country)* of residence: CH

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

- [ ] Further applicants and/or (further) inventors are indicated on another continuation sheet

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (*mark the applicable check boxes, at least one must be marked*)

Regional Patent

☒ AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☒ EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

☒ AL Albania
☒ AM Armenia
☒ AT Austria
☒ AU Australia
☒ AZ Azerbaijan
☒ BA Bosnia and Herzegovina
☐ BB Barbados
☒ BG Bulgaria
☒ BR Brazil
☐ BY Belarus
☒ CA Canada
☒ CH and LI Switzerland and Liechtenstein
☒ CN China
☒ CU Cuba
☒ CZ Czech Republic
☒ DE Germany
☒ DK Denmark
☒ EE Estonia
☒ ES Spain
☒ FI Finland
☒ GB United Kingdom
☒ GE Georgia
☒ GH Ghana
☒ GM Gambia
☐ GW Guinea-Bissau
☒ HU Hungary
☒ ID Indonesia
☒ IL Israel
☒ IS Iceland
☒ JP Japan
☒ KE Kenya
☐ KG Kyrgyzstan
☒ KP Democratic People's Republic of Korea
☒ KR Republic of Korea
☐ KZ Kazakhstan
☐ LC Saint Lucia
☒ LK Sri Lanka
☒ LR Liberia
☒ LS Lesotho
☒ LT Lithuania
☒ LU Luxembourg
☒ LV Latvia
☐ MD Republic of Moldova
☐ MG Madagascar
☒ MK The former Yugoslav Republic of Macedonia
☐ MN Mongolia
☐ MW Malawi
☒ MX Mexico
☒ NO Norway
☒ NZ New Zealand
☒ PL Poland
☒ PT Portugal
☒ RO Romania
☒ RU Russian Federation
☒ SD Sudan
☒ SE Sweden
☒ SG Singapore
☒ SI Slovenia
☒ SK Slovakia
☒ SL Sierra Leone
☐ TJ Tajikistan
☐ TM Turkmenistan
☒ TR Turkey
☐ TT Trinidad and Tobago
☒ UA Ukraine
☒ UG Uganda
☒ US United States of America
☐ UZ Uzbekistan
☒ VN Viet Nam
☒ YU Yugoslavia
☒ ZW Zimbabwe

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

☐ .....
☐ .....
☐ .....

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of _____

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15 month time limit.)*

Box No. VI PRIORITY CLAIM — Further priority claims are indicated in the Supplemental Box ☐

The priority of the following earlier application(s) is hereby claimed:

	Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1)	EP	21.02.1997	97102837.8	European Patent Office
item (2)				
item (3)				

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

☒ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s): (1)

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):* ISA /

Earlier search *Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:*

Country (or regional Office): Date *(day/month/year)*: Number:

Box No. VIII CHECK LIST

This international application contains the following number of sheets:

1. request	:	4 sheets
2. description	:	43 sheets
3. claims	:	4 sheets
4. abstract	:	1 sheets
5. drawings	:	9 sheets
Total	:	61 sheets

This international application is accompanied by the item(s) marked below:

1. ☐ separate signed power of attorney
2. ☐ copy of general power of attorney
3. ☐ statement explaining lack of signature
4. ☐ priority document(s) *identified in Box No. VI as item(s):*
5. ☒ fee calculation sheet
6. ☒ separate indications concerning deposited microorganisms
7. ☒ nucleotide and/or amino acid sequence listing (diskette)
8. ☒ other *(specify)*: See attached list I

Figure No. 7 of the drawings (if any) should accompany the abstract when it is published.

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Patentanwalt Konrad Schaefer

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority specified by the applicant: ISA /
6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau

This sheet is not part of and does not count as a sheet of the international application

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No

Date stamp of the receiving Office

Applicant's or agent's file reference: 01110eppc

Applicant: Kanton Zürich
vertreten durch die Erziehungsdirektion

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . 200,-- T

2. SEARCH FEE . . . . . 2200,-- S

International search to be carried out by _____

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 61 sheets.

first 30 sheets . . . . . 800,-- b_1

31 remaining sheets x 19 additional amount = 589,-- b_2

Add amounts entered at b_1 and b_2 and enter total at B . . . . 1389,-- B

Designation Fees

The international application contains 61 designations.

11 number of designation fees payable *(maximum 11)* x 184,-- amount of designation fee = 2024,-- D

Add amounts entered at B and D and enter total at I . . . . . 3413,-- I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

FEE FOR PRIORITY DOCUMENT . . . . . 60,-- P

5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P, and enter total in the TOTAL box . . 5873,-- TOTAL

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☐ authorization to charge deposit account (see below)
☐ cheque
☐ postal money order
☐ bank draft
☐ cash
☐ revenue stamps
☐ coupons
☐ other *(specify)*:

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ EPO

☒ is hereby authorized to charge the total fees indicated above to my deposit account.

☒ is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☒ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account

EPO 28000854
Deposit Account Number

17.02.1998
Date *(day/month/year)*

Signature

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/00917

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/70 C07K16/18 C12N5/20 C07K14/47 C12N15/06
C12N1/21 C12N5/10 G01N33/577 G01N33/68 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X,O	C. KORTH ET AL.: "Characterization of native and recombinant prion protein isoforms by differential exposure of antibody epitopes." SOCIETY FOR NEUROSCIENCE, ABSTRACTS, vol. 22, no. 1-3, 16 - 21 November 1996, page 2159 XP002036864 see abstract 844.3 ---	1-7, 32-34
X	R. KASCSAK ET AL.: "The role of antibodies to PrP in the diagnosis of transmissible spongiform encephalopathies." DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, vol. 80, 1993, BASEL, pages 141-151, XP002036865 see the whole document --- -/--	1-7, 32-34

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

Special categories of cited documents

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 June 1998	15. 07. 1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Nooij, F

Form PCT/ISA/210 (second sheet) (July 1992)

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 23432 A (NEW YORK UNIVERSITY ET AL.) 25 November 1993 see the whole document ---	1,3, 32-34
A	A. PARAF: "Scrapie and bovine spongiform encephalopathy: immunological properties and diagnosis for food products." LAIT, vol. 76, no. 6, November 1996, PARIS, pages 571-578, XP002036866 see the whole document ---	1-39
A	S. PRUSINER ET AL.: "Immunologic and molecular biologic studies of prion proteins in bovine spongiform encephalopathy." JOURNAL OF INFECTIOUS DISEASES, vol. 167, March 1993, pages 602-613, XP002036867 see the whole document ---	1-39
A	M. CANN ET AL.: "Antibody fragments to PrP generated using phage display technology." JOURNAL OF CELLULAR BIOCHEMISTRY, SUPPLEMENT, vol. 18 part D, 1994, page 198 XP002036868 see abstract T304 ---	1-39
A	B. SCHREUDER ET AL.: "Preclinical test for prion diseases." NATURE, vol. 381, no. 6583, 13 June 1996, LONDON, page 563 XP000579899 see the whole document ---	1-39
A	S. KRASEMANN ET AL.: "Induction of antibodies against human prion proteins (PrP) by DNA-mediated immunization of PrP0/0 mice." JOURNAL OF IMMUNOLOGICAL METHODS, vol. 199, no. 2, 15 December 1996, AMSTERDAM, pages 109-118, XP002036869 see the whole document ---	1-39
A	WO 93 11155 A (PROTEUS MOLECULAR DESIGN LTD.) 10 June 1993 see the whole document ---	1-39

-/--

INTERNATIONAL SEARCH REPORT

National Application No
PCT/EP 98/00917

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No
P,X	C. KORTH ET AL.: "Prion (PrPSc)-specific epitope defined by a monoclonal antibody." NATURE, vol. 390, no. 6655, 6 November 1997, LONDON, GB, pages 74-77, XP002069611 see the whole document	1-8, 10-12, 14,15, 17-39
P,X	WO 97 10505 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 20 March 1997 see examples see claims	1-4, 24-27, 29,32,33

Form PCT/ISA 210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

.ational application No
PCT/EP 98/00917

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 36 and 38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest

[ ] No protest accompanied the payment of additional search fees.

INT[redacted]N. IONAL SEARCH REPORT

Information on patent family members

tional Application No
PCT/EP 98/00917

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9323432 A	25-11-1993	AU 4376093 A	13-12-1993
WO 9311155 A	10-06-1993	AU 675053 B	23-01-1997
		AU 3089292 A	28-06-1993
		CA 2124953 A	10-06-1993
		EP 0616613 A	28-09-1994
		JP 7501798 T	23-02-1995
		NZ 246059 A	28-08-1995
		ZA 9209392 A	27-07-1993
WO 9710505 A	20-03-1997	AU 7073596 A	01-04-1997